on support systems both from the institution and from colleagues. My department in particular is very supportive of junior faculty, regardless of gender.

Collaboration is now the foundation of research. For some early career researchers, especially women, it might be intimidating to make that first move and initiate conversation that might lead to collaboration. How did you manage this?

Establishing collaborations can be intimidating for young scientists, whether male or female. I don't know if there is any difference for either. It's all about confidence and it takes time to build that confidence. I got around this by collaborating with people I knew and liked, and I still tend to do that. I think collaborating with people you are comfortable with makes life easier – it helps with the flow of ideas, it can bring out creativity you might otherwise repress, and it generates a fun environment where everyone can perform at their best – it makes science more productive.

What can institutions do to support women in science?

There needs to be institutional support for women, but this is something that also needs change at a societal level. Institutions should encourage and foster mentorship, and make sure that women have the same confidence in themselves as men do; they need to give them credit for their good work.

Academia can influence education and how society works overall – this is a long-term goal that might take a few decades. It is important to change the mentality so that these types of questions don't need to be asked any more!

If you were not a scientist, what would your alternative career be?

I have two things that I would love to do. I would love to be a musician and, in particular, write music. I play the keyboard and make up some things; but if I could, I would invest more time in this and create music.

I've also always liked the idea of being an archaeologist, and digging things up. I love the idea of discovery. Discovery and creativity really are my driving motivations. When I think of why I love what I do now, I realize it's because I can be creative; I can try to prove hypotheses right or wrong. I get to ask questions and find answers – and it's a privilege.

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Science & Society

The Hitchhiking Parasite: Why Human Movement Matters to Malaria Transmission and What We Can Do About It

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The failure of the Global Malaria Eradication Program (GMEP) during the 1960s highlighted the relevance of human movement to both re-introducing parasites in elimination settings and spreading drug-resistant parasites widely. Today, given the sophisticated surveillance of human movement patterns and key traveler groups, it is hoped that interventions can be implemented to protect and treat travelers, prevent onward transmission in low transmission settings, and eliminate sources of transmission, including sources of drug-resistant parasites.

The Role of Human Movement in Disease Transmission

The relevance of human movement to disease transmission has gained increased attention in recent years following a string of outbreaks, including Zika, Ebola, and H1N1 influenza. The rapid international spread of these diseases highlights the role of movement in transmission, and the role of intensive control measures, such as quarantine and contact tracing, in preventing their spread. When it comes to endemic diseases, such as malaria, the relevance of human movement to disease transmission is twofold: (i) it enables transmission to persist in lower transmission settings; and (ii) it facilitates the spread of drug-resistant parasites.

First, because significant funds are being invested in global malaria control, prevalence is declining overall, but significant heterogeneity in transmission remains at all spatial scales [1]. Within this context, an understanding of human movement is essential to determine how best to optimize control strategies by targeting: (i) sources of transmission; (ii) conduits of travel by high-risk travelers; and (iii) receptive locations vulnerable to outbreaks as a result of importation [2]. While human movement is ubiquitous across transmission settings, it is a particular concern in locations where local transmission has been reduced but the environment is still conducive to transmission [1,3]. In these settings, an increasing proportion of remaining transmission is often due to parasite importation and, hence, malaria programs must address this to prevent resurgence.

Second, human movement is the major driver of the spread of drug-resistant parasites. Indeed, parasite resistance to the

current first-line therapy for malaria, artemisinin combination therapy drugs (ACTs), has recently been observed in the Greater Mekong Subregion (GMS) [4]. Spread of this resistance to sub-Saharan Africa, where the burden of malaria is highest, would be devastating. The importance of human movement to the spread of drug-resistant parasites is illustrated by the failure of the GMEP during the 1960s, which was partly attributed to the role of human movement in both reintroducing parasites in elimination settings and spreading parasites resistant to chloroquine, the main antimalarial drug at that time [5].

Here, we discuss: (i) how we can achieve a deeper understanding of human movement and key traveler groups of relevance to parasite dispersal through integrated surveillance activities; and (ii) how we can maintain recent gains in malaria control and prevent the spread of drug-resistant parasites, given knowledge of human movement patterns.

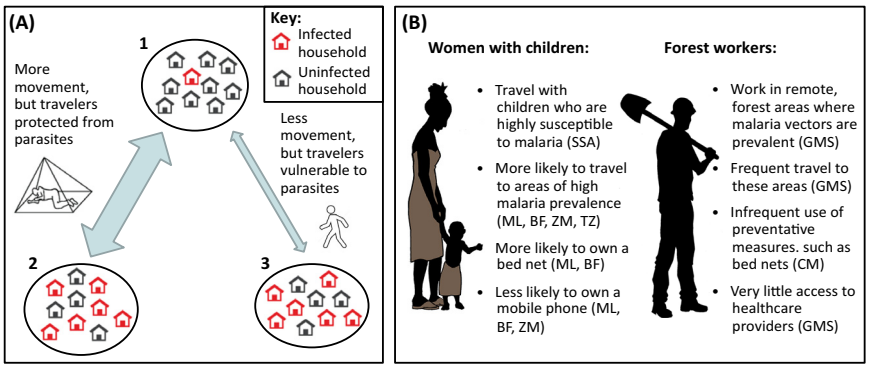

Figure 1. Parasites on the Move. (A) Thought experiment demonstrating the difference between human movement and parasite movement. A low prevalence area (1) exchanges travelers with two high prevalence areas (2 and 3). Movement between (1) and (2) accounts for most of the human movement in and out of (1), but little of the parasite movement because the travelers use effective personal protection measures. Less human movement occurs between (1) and (3), but more parasite movement because the travelers are particularly vulnerable to malaria infection. Therefore, it is important to know the risk status of travelers in addition to movement rates. (B) Traveler groups found to have elevated risk status for malaria: women with children in sub-Saharan Africa (SSA), specifically in Mali (ML), Burkina Faso (BF), Zambia (ZM), and Tanzania (TZ); and forest workers in the greater Mekong subregion (GMS), specifically in Cambodia (CM). These traveler groups are less frequently captured in some data sets due to reduced cell phone ownership and access to healthcare providers.

Surveillance of Humans and Parasites

For many malaria programs, the only data source available to understand parasite movement is the travel history of people diagnosed with malaria in health facilities. Shortcomings of this approach are: (i) the parasite may have been contracted before or after the trip; (ii) many imported cases are missed by passive reporting systems because they are asymptomatic or simply not reported; and (iii) some key traveler groups, such as forest workers in Southeast Asia, are under-represented because they are less likely to attend health facilities. Furthermore, the timeframe used to determine whether an infection is imported varies between 18 days and 3 months, depending on the country, making it difficult to compare malaria burdens due to importation [2].

Several new methods and data sets are now becoming available to better characterize human and parasite movement [6]. Parasite genetic sequences provide a direct window into parasite movement and can be used to infer whether a given infection is the result of local transmission or importation based on relatedness to locally circulating strains [7]. Novel methods are also being developed to infer networks of transmission based on accumulated mutations in parasite genetic sequences; however, these methods must be validated against other data sets to confirm their accuracy.

Several studies have used GPS loggers to monitor human movement. These provide high-resolution data documenting fine-scale movements and can potentially be linked to parasite status; however, they are limited by the number of people they can monitor [8]. Cell phone call detail records (CDRs) are less well resolved than GPS logger data, but can be used to monitor the movements of much larger populations, albeit with biases due to cell phone ownership and usage patterns [9]. Census-derived migratory movements have been shown to correlate with CDR-derived short-term movements in Mesoamerica, suggesting that census data could serve as a predictor for human movement at multiple scales [10]. Furthermore, detailed surveys recording movement patterns, demographic data, and cell phone usage behavior can help to correct for biases inherent in these data sets and to classify traveler groups with distinct malaria risk characteristics [11]. Each of these data sets is associated with its own biases and a research agenda is needed to understand those biases and prioritize surveillance protocols that will be operationally useful.

While there are several different data sources to better understand human movement, patterns of human movement do not necessarily reflect patterns of parasite movement. This is illustrated in Figure 1A, where, for example, if human movement is assumed to be equivalent to parasite movement, then human movement data will suggest that malaria importation mostly originates from population 2; however, it may in fact be dominated by human movement from population 3 due to the susceptibility of these travelers to mosquito bites. Evidence from surveys in sub-Saharan Africa and Southeast Asia

suggests that there are groups of high-risk travelers with unique movement patterns [11,12] (Figure 1B). Therefore, one fundamental output from a surveillance program is to identify key groups whose movements contribute disproportionately to sustaining parasite transmission and/or the dispersal of drug-resistant parasites.

Key Traveler Groups

Characteristics of key traveler groups include vulnerability to mosquito bites, travel frequency, origins, and/or destinations where (and when) malaria parasite prevalence is high, and poor access to health facilities. In the GMS, where ACT-resistant parasites have emerged, studies highlight forest workers as a key highly mobile group of relevance to malaria transmission [12] (Figure 1B). The main malaria vectors in Southeast Asia are associated with forest environments, and forest workers frequently travel to these areas, often without protective measures. They also have relatively poor access to health services, meaning that, when they are infected, they tend to remain infected for a long period of time. This has led the WHO to recommend that interventions be targeted towards this group to prevent the spread of ACT-resistant parasites [4].

In sub-Saharan Africa, a recent survey in Mali, Burkina Faso, Zambia, and Tanzania [11] found that women traveling with children are a remarkably consistent group of travelers of relevance to malaria transmission (Figure 1B). While this group is more likely to own a bed net in some countries, they are significantly more likely to travel to areas of high malaria prevalence in all countries surveyed. The children that accompany them are particularly susceptible to malaria infection and have less developed immune systems, enabling this traveler group to contribute greatly to parasite dispersal. The same survey highlighted youth workers as a key traveler group of relevance to parasite dispersal in Mali, largely due to their agricultural labor trips coinciding with the rainy season, when malaria risk is highest [11].

Enhanced Malaria Control through Understanding Movement

A key to maintaining recent gains in malaria control in low transmission settings and progressing to elimination is to realize that imported infections can be minimized at any of four stages of human movement: during outgoing travel; at the high transmission setting (source); during return travel; and upon return to the low transmission setting [2] (Figure 2).

Outgoing travelers can be protected during their trip by providing them with personal protection measures, such as long-lasting insecticide-treated nets (LLINs), antimalarial drugs, such as ACTs, and prophylactic drugs with a long preventative period. Active surveillance of high-risk return travelers, for example at ports and border crossings, can increase the chances that infected travelers are clear of parasites upon arrival. In low transmission settings, the goal is to minimize the onward transmission of imported cases through active surveillance and rapid response measures. Response measures may include testing and/or treating individuals who traveled with the imported case. Finally, malaria importation can be addressed by reducing transmission at sources of transmission [2], which are locations where malaria is endemic and from where parasites may be exported to other areas.

Questions arise as to how best prioritize interventions at each of these stages in the context of existing human and parasite movement patterns. As malaria prevalence declines, there is potential for reduced national investment in malaria control, so it is essential for programs to carefully allocate resources to the most impactful interventions. Where transmission can be prevented at its source, this should be prioritized, because it will have downstream effects on reducing the need for interventions in receptive, low transmission settings and along conduits of travel [13]. When sources are in other countries, regional initiatives may be required, and ways to incentivize the main exporting countries should be explored. Within national boundaries, human movement data are needed to inform which sources are exporting cases to receptive,

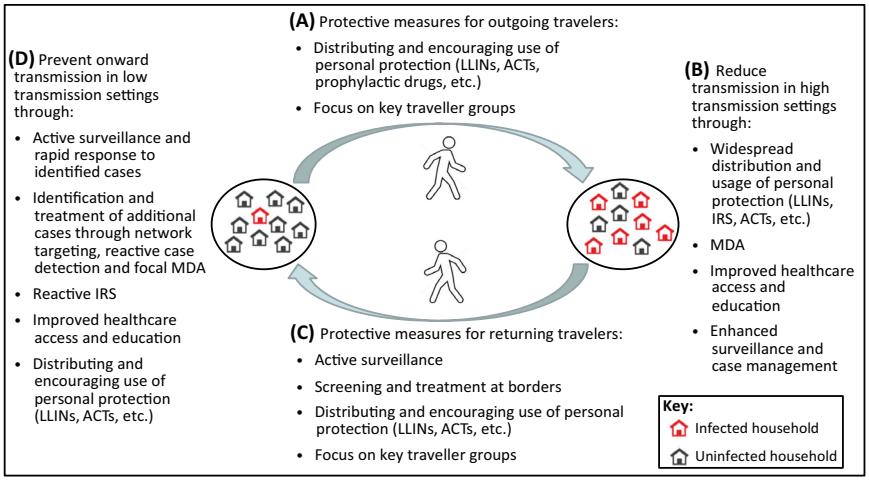

Figure 2. Interventions to Reduce Malaria Transmission in Low Transmission Settings. Interventions may be designed to: (A) provide protective measures to outgoing travelers; (B) reduce transmission in high transmission settings (sources); (C) provide protective measures and carry out screening and treatment for return travelers; and (D) target imported primary and secondary infections in the low transmission setting. Abbreviations: ACT, artemisinin-based combination therapy drugs; IR, indoor residual spraying with insecticides; LLIN, long-lasting, insecticide-treated net; MDA, mass drug administration.

low transmission areas. For small parasite importation rates in low transmission areas, it may be adequate to engage in interventions targeted towards key traveler groups and responses focused around detected cases; however, for higher parasite importation rates, community-level interventions may be preferable. The receptivity of the environment to onward transmission is another key determinant of intervention choice.

Strategies for preventing the spread of drug-resistant parasites are similar if we imagine the population with drug-resistant parasites as a source. Intensive efforts to eliminate the source of infection will prevent the exportation of drug-resistant parasites elsewhere [4]. Indeed, this is the approach being taken in the GMS [14]. For drug-resistant parasites, even asymptomatic infections should be targeted. Key traveler groups, such as forest workers, are most likely to spread drug-resistant parasites and, hence, should be provided with protective measures and actively surveilled, screened, and treated.

Due to the huge variety of human movement patterns in differing geographies, the optimal combination of interventions to reduce malaria importation and the spread of drug-resistant parasites may vary greatly by location [2]. A common research agenda is required to determine how best to address this through: (i) a deep understanding of human movement patterns, particularly of key traveler groups; and (ii) an integrated framework for determining optimal intervention strategies, taking into account financial, operational, and technical constraints.

The cross-border nature of human movement requires this to be a collaborative effort because, in many cases, the sources may be international. An increasing number of regional and cross-border initiatives are emerging that provide encouragement for international collaborations; for example, the WHO Strategy for Malaria Elimination in the GMS, which includes Cambodia, Laos, Myanmar, Thailand, Vietnam, and Yunnan Province in China, and the E8 initiative in southern Africa, which includes Botswana, Namibia, South Africa, Swaziland, Angola, Mozambique, Zambia, and Zimbabwe [14,15]. The activities of the E8 initiative, for instance, include developing a shared database to track cases regionally, setting up health posts in areas with poor access to health care, and deploying response teams along national borders. It is hoped that, with a collaborative spirit and advances in surveillance and intervention technology, the original goals of the GMEP will be achieved in this era.

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Spotlight

Leishmania DNA Replication Timing: A Stochastic Event?

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For eukaryotic genomes, DNA synthesis initiates at multiple discrete regions known as replication origins in a dynamic yet regulated manner to ensure genomic stability. Two recent studies using different approaches reveal few *Leishmania* origins and that origin firing may proceed in a mainly stochastic manner.

Trypanosomatids are an early diverging branch of eukaryotic life with many notable members that cause devastating diseases in both animals and humans including Chagas disease, sleeping sickness, and leishmaniasis. DNA replication mechanisms in these parasites has gained prominence with a handful of key reports revealing that this essential process has several divergent features that might serve as potential drug targets. These include DNA replication initiation proteins of the origin recognition complex (ORC) and an unprecedented level of functional interaction between transcription and DNA replication [1]. Despite recent advances, work on trypanosomatid DNA replication is still at an early stage with many remaining questions, including how replication